Mr. Coberly/ Reviews

ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D. C. 20460

004678

Date: February 23, 1973

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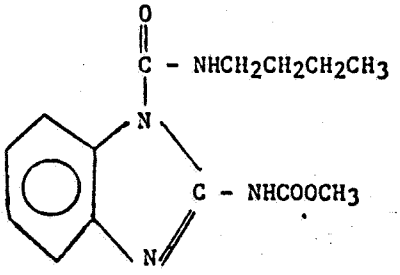
To: Mr. Lee TerBush, Acting Chief
Coordination Branch
Registration Division

Registration No.	:	352-354
Product Name	:	Benlate Benomyl Fungicide
Registrant	:	E.I. du Pont de Nemours & Co. (Inc.) Wilmington, Delaware
Chemical Name	:	Methyl 1-(butylcarbamoyl)-2-benzimidazolecarbamate
Chemical Structure	:	
Use	:	Fungicide for control of certain diseases of peanuts, sugar beets, beans (snap), pineapple, sugarcane, roses, flowers, and ornamentals.
Application Method	:	Spray with ground equipment or dip.

BACKGROUND INFORMATION

Related Petitions	:	CF0906, OG0936, OF1000, OF1010, 1G1033, 1F1038, 1F1145, 2F1192, 2G1197, 2F1218, 2H5004, 2H5009, 2F1234, 2E1239 and 2F1240.

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Existing Tolerances: 40 CFR 180.294

15 ppm - apricots, cherries, nectarines, peaches, and plums
2 ppm - snap beans (succulent)
1 ppm - bananas - 0.2 ppm (negligible) on banana pulp after the peel is removed
1 ppm - cucumbers, melons, summer squash, and winter squash
0.2 ppm - peanuts and sugar beet roots

TOXICITY DATA

The following tests were reviewed in memos of Dr. M.L. Quaife dated March 25, 1970 (0F0906, 0G0936), May 3, 1971 (0F0906, 0F1000, 1F1010, 1F1033, 1F1045), and January 3, 1972 (1F1145, 2F1192, 2G1197):

Acute oral - Rat	LD_{50} > 9590 mg/kg
Acute dermal - Rabbit	LD_{50} >10000 mg/kg
Acute inhalation - Rat	LC_{50} >1.37 mg/liter air
*90-day feeding study - Rat	Systemic NEL 500 ppm
**90-day feeding study - Dog	Systemic NEL 500 ppm
***2-year feeding study - Rat	Systemic NEL 2500 ppm
***2-year feeding study - Dog	Systemic NEL 500 ppm
***3-generation reproduction - Rat	Systemic NEL 100 ppm
Teratology - Rat	Negative at 5000 ppm
Teratology - Rabbit	Negative at 500 ppm
Acute oral - Rat (metabolite*)	LD_{50} >17 g/kg
90-day feeding study - Rat (metabolite*)	Systemic NEL 2500 ppm
3-generation reproduction Rat (metabolite*)	Systemic NEL 2500 ppm

[redacted]

***both samples (* and **) were used

Other data contained in our files plus Pesticide Petition No. 0F0906 include the following:

Acute Rat Oral LD_{50} (50% WP)	greater than 10,000 mg/kg
Acute Rat Oral LD_{50} (technical	greater than 10,000 mg/kg
Acute Rabbit Oral ALD (50% WP)	greater than 3,400 mg/kg
Acute Rabbit Dermal LD_{50} (50% WP)	greater than 10,000 mg/kg
Acute Rat Inhalation LC_{50} (50% WP)	greater than 2 mg/L

Primary Skin Irritation In Guinea Pig (50% WP) - Mild irritation

Rabbit Eye Irritation (50% WP) - Mild irritation

Sensitization In Guinea Pig (50% WP) - Mild sensitization noted

Acute Rat LC_{50} - Hazleton Lab October 18, 1968

The material tested was identified as fungicide 1991 - 50% active ingredient.

Six male rats were used per level of 0.27, 1.39 and 4.01 mg/L. Length of exposure was four hours.

Results

Two cases of slight aspermatogenesis and two cases of a moderate reduction in spermatogenic activity were observed at the 0.27 mg/L level. One case of slight to moderate aspermatogenesis and one case of reduction in spermatogenic activity were noted at the 1.39 mg/L level. Two cases of severe aspermatogenesis and one case of reduced spermatogenic activity were evident at 4.01 mg/L. The incidence and severity of inflammatory lesions in the lung and inflammatory cell infiltration into the submucosa of the trachea were increased at the 4.01 mg/L level.

21 Day Rat Inhalation - Haskell Lab - April 30, 1970

The material tested was identified as "commercial" formulation of 53.5% methyl 1-(butylcarbamoyl)-2-benzimidazolecarbamate [redacted]

Ten Charles River male rats were exposed per air concentration of 0.02 and 0.2 mg/L for four hours a day. Half the animals were sacrificed after the 15th exposure, the remainder at 14 day post treatment.

Observations and tests included gross and histopathologic examination of the lung, liver, spleen, kidney, testes, and bone marrow; clinical signs and body weight.

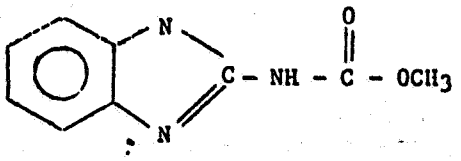
Results

No clinical or histopathologic effects attributable to Benlate were noted.

100-66 14 Day Rat Intubation (Unformulated chemical): 100-66

Adverse tissue alterations were observed at 3400 mg/kg/day in the stomach, liver and testes. No significant histological changes were noted at 200 mg/kg/day.

2-Benzimidazolecarbamic acid, Methyl Ester



66-66 Rat Oral ALD - Haskell Lab - July 15, 1966

The material tested was identified as 2-Benzimidazolecarbamic acid, methyl ester.

One male ChR-CD rat was used per level in a range of from 200-17,000 mg/kg. Material was administered as a 5-30% suspension in peanut oil.

Results

ALD is greater than 17,000 mg/kg. Levels of 1000 mg/kg and above exerted an adverse effect upon the testis.

65-65 Rat Oral ALD - Haskell Lab - August 20, 1965

The material tested was identified as 2-Benzimidazolecarbamic acid, methyl ester (INE-965).

ChR-CD male rats were tested in a dose range of from 670 to 11,000 mg/kg. Material was given as a 25% suspension in peanut oil.

Results

ALD is greater than 11,000 mg/kg. Levels of 1500 mg/kg or greater caused depression of spermatogenesis.

Fourteen Day Rat Intubation- Haskell Lab - July 15, 1966

The material tested was identified as 2-Benzimidazolecarbamic acid, methyl ester.

Six male ChR-CD rats were used per level of 200 and 3400 mg/kg. Material was administered as a suspension in peanut oil. A total of ten treatments were given. Half the animals were sacrificed four hours post treatment and the remainder at 14 days post treatment.

Observations and tests for effects included mortality, body weight, histological examination of the liver, kidney, spleen, bone marrow, thyroid, lung, GI tract, brain, thymus and pancreas from the control and 3400 mg/kg/day animals.

Results

Two deaths occurred at the 3400 mg/kg/day level due to the cumulative oral toxicity. Edema and focal necrosis of the duodenum, reduction in the blood-forming elements of the bone marrow and a decrease in the large globular-shaped vacuoles located centrolobularly in the liver were evident at the high level. Mild diarrhea and body weight loss were also noted at the high level.

Three of six animals at 200 mg/kg/day showed slight adverse changes in the testis.

7-65 Fourteen Day Rat Intubation - Haskell Lab - August 20, 1965

The material tested was identified as 2-Benzimidazolecarbamic acid, methyl ester (INE-965).

Six Charles River-Wistar male rats were used at the level of 5000 mg/kg/day. Material was administered as a 25% suspension in peanut oil for a total of ten doses. Half the rats were sacrificed at three hours post treatment, the remainder at 10 days post treatment.

Results

No mortality occurred. Toxic signs displayed were body weight loss, weakness, loss of hair and polyuria. Pathologic changes included small testes and abolished spermatogenesis.

PRESENT ACTION

P.C. Critchlow requested a review of the precautionary labeling for Benlate in reference to the new use patterns accepted in Petitions 1F1033, 1F1145, 1F1192, 2F1212, 2F1240, 2F1289 and 2F1290.

CONCLUSION

The aforelisted toxicity data support the judgement that the proposed usage pattern will not create an undue human health hazard.

Robert D. Coberly, Biologist
Toxicology Branch
Registration Division

cc:
Ecological Effects Branch
Division Reading File
PCCritchlow
GEWhitmore
Branch Reading File

RDCoberly/km 02-27-73